

REMARKS

Applicants respectfully request that the foregoing amendments to Claims 7, 8, 11, 12, 14, 16-18 and 23 be entered in order to avoid this application incurring a surcharge for the presence of one or more multiple dependent claims.

Respectfully submitted,

By



Date April 20, 2001

FOLEY & LARDNER  
Washington Harbour  
3000 K Street, N.W., Suite 500  
Washington, D.C. 20007-5109  
Telephone: (202) 672-5427  
Facsimile: (202) 672-5399

Bernhard D. Saxe  
Attorney for Applicant  
Registration No. 28,665

VERSION WITH MARKINGS TO SHOW CHANGES MADE

6. (Amended) The method of claim 5, wherein the location and orientation of a side-chain of each said amino acid residue of said framework protein and the location and orientation of a side-chain of each of said two or more amino acid residues of said sample protein is simplified as a respective  $\text{C}\alpha\text{-C}\beta$  vector.

7. (Amended) The method of [any one of Claims 1, 3, 4 or 6] claim 1, wherein the  $\text{C}\alpha\text{-C}\beta$  vector is in the form of a distance matrix representation.

8 (Amended) The method of Claim 1 [or Claim 2], further including the step of modifying an amino acid sequence of said framework protein which corresponds to a hit, by substituting at least one amino acid residue thereof with at least one amino acid residue of said sample protein to thereby create a modified framework protein.

11. (Amended) The method of [any of Claims 8-10] claim 8, wherein the modified framework protein has greater stability than said sample protein.

12. (Amended) The method of [any of Claims 8-11] claim 8, wherein the modified framework protein has increased structural similarity to said sample protein.

14. (Amended) The method of [any preceding] claim 14, wherein the sample protein is a cytokine.

16. (Amended) The method of Claim 1 [or Claim 2], wherein at step (iii) the hits are ranked according to structural similarity with said sample protein.

17. (Amended) The method of Claim 1 [or Claim 2], wherein searching at step (iii) includes:

(a) identification of said hits by clique detection;

(b) filtering of said hits identified at step (a).

18. (Amended) A modified framework protein produced according to the method of [any one of Claims 9-15] claim 9.

23. (Amended) The engineered protein of [any one of Claims 20-22] claim 20, wherein said another protein is a cytokine.

1002570535.1